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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/527,028	03/16/00	VERIAC S	0198/053

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EXAMINER	
GABEL,G	
ART UNIT	**PAPER NUMBER**
1641	3

DATE MAILED: 06/28/01

Pl ase find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/527,028	VERIAC ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

2. The Information Disclosure Statement (PTO-1449) filed 6/14/00 in Paper No. 2 is acknowledged. Reference AO was not considered because neither an English translation nor a statement of relevancy was provided therefor.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 preamble is vague and indefinite in reciting "for determination of leucocytes and of basophil ...," because it is unclear as to whether Applicant intends to encompass quantitative measure of both elements set forth or differential identification thereof.

Claim 1, part 1 is indefinite in reciting "selectively" because the term "selectively" is a subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 3 recites improper Markush language and format in reciting "selected from the group comprising". Change to "selected from the group consisting of" for proper Markush language.

In claim 3, the symbol " / " renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by " / "), thereby rendering the scope of the claim unascertainable. Specifically, it is unclear as to whether the symbol " / " intends to mean selective, i.e. potassium chloride **or** hydrochloric acid; or inclusive, i.e. potassium chloride **and** hydrochloric acid. Please clarify. See also claim 11.

Claim 4 recites improper Markush language and format in reciting "selected from the group comprising". Change to "selected from the group consisting of" for proper Markush language.

Claim 4 lacks antecedent support in reciting "the primary amines, the acetates".

Claim 4 lacks antecedent support in reciting "the quaternary ammonium salts".

Claim 4 lacks antecedent support in reciting "the amides".

Claim 9 recites improper Markush language and format in reciting "selected from the group comprising". Change to "selected from the group consisting of" for proper Markush language.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takarada et al. (US 5,677,183) in view of Hamaguchi et al. (US 5,389,549).

Takarada et al. disclose a reagent system, a first reagent and a second reagent for identifying and classifying leucocytes including basophil (see column 8,lines 37-56). Specifically, the first reagent for classifying leucocytes comprises a cationic detergent (surfactant) such as quaternary ammonium salt. The cationic detergent is present in sufficient amount to lyse erythrocytes and damage or porify leucocyte cell membrane, i.e. 0.5 - 300 g/l (see column 1, lines 53-55 and column 2, line 46-to column 3, line 26). The first reagent further also comprises a buffer such as phthalic acid or citric acid for adjusting pH to a desired pH of <3.0, preferably 2.0 (see column 5, lines 1-8). The first

reagent may further contain alkali metal salts and inorganic salts such as sodium chloride and potassium chloride (see column 5, lines 9-24). The second reagent is used for measuring basophils which also includes a cationic detergent such as quaternary ammonium salt, a buffer for maintaining the pH at 2.5 - 4.0 such as phthalic acid or citric acid, a nonionic surfactant, and also alkali metal or inorganic salts (see column 5, lines 38-45 and column 7, line 44 to column 8, line 36).

Takarada et al. differ in failing to disclose a nitrogenous compound in the reagent system.

Hamaguchi et al. disclose a reagent system for counting and classifying leucocytes including basophil and lysing erythrocytes (see Abstract and column 12, lines 51-66). Specifically, the reagent comprises a blood diluent including a phosphate buffer, sodium chloride, and a hyperosmotic or cytolytic agent; an ionic detergent (surfactant); an nonionic detergent; and a nitrogenous compound (solubilizing agent) for use in reducing the sizes of monocytes in leucocytes (see column 7, line 40 to column 8, line 25 and Example 1). The solubilizing agent includes nitrogenous compounds such as thiourea or 1,3- dimethylurea (see column 8, lines 26-35). The reagent buffer maintains the pH at 1.5-5.0 (see column 10, lines 24-28). In Example 4, Hamaguchi et al. disclose the reagent enabled for basophil measurement comprising a buffer having potassium phthalate, hydrochloric acid, nitric acid, and a lysing agent at an acidic pH of 3.0. Specifically, Hamaguchi et al. disclose that when a solubilizing agent is incorporated into a lysing agent or diluent, the solubilizing agent selectively promotes the action of the lysing reagent into monocytes. Hamaguchi et al. also specifically

disclose that such selective action of solubilizing agents to monocytes is also effective with all other reagents used in leucocyte classification (see column 19, lines 22-54).

One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in incorporating the solubilizing agent / nitrogenous compound as taught by Hamaguchi into the reagent system taught by Takarada because Hamaguchi specifically disclosed and suggested applicability of such agent with all other reagents used in leucocyte classification such as the reagent system taught by Takarada.

Takarada et al. and Hamaguchi et al. differ in failing to disclose the specific concentration parameters of elements recited in claims 10 and 11.

It is, however, maintained that the concentration parameters such as detergent [0.2-20 g/l] and nitrogenous compound [0.1-10 g/l] recited in claim 10 and potassium chloride [5-15 g/l], 1,3- dimethyl-2- thiourea [0.5-5 g/l], dodecyltrimethylammonium chloride [0.5-5 g/l], and potassium hydrogen phosphate / HCl [1.0-10 g/l] which are recited in claim 11, are all result effective variables which the prior art references have shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-

237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 10 and 11 are for any particular purpose or solve any stated problem and the prior art teaches that the different reagent elements and parameters often vary according to the sample being analyzed and parameters appear to work equally as well; absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the Takarada and Hamaguchi by normal optimization procedures known in the leucocyte differentiation art.

5. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakata et al. (US 5,538,893) in view of Hamaguchi et al. (US 5,389,549).

Sakata et al. disclose a reagent system for analyzing and classifying leucocytes including basophil which is capable of determining cell size and morphological features of leucocytes (see Abstract and column 2, lines 18-39). Specifically, the reagent comprises a nonionic detergent, a buffer for adjusting the pH to 2.5 - 4.0, and a cationic detergent (surfactant) such as quaternary ammonium salt for complete lysis of erythrocytes and baring the nuclei of granulocytes other than basophil (see column 4, lines 21-59). The reagent buffer used includes citric acid and tartaric acid as well as alkali metal hydroxides such as sodium hydroxide and potassium hydroxide for adjusting pH to a desired pH of 2.0 - 5.0 (see column 5, lines 25-40). The surfactants

and the buffer can be prepared and mixed at desired ratios (see column 5, lines 44-63). The reagent system may further contain alkali metal salts and inorganic salts such as sodium chloride and potassium chloride (see column 6, lines 1-6). Sakata et al. disclose that at appropriate concentrations, cell lysing is exhibited and lymphocytes and monocytes immature granulocytes and basophils which include a large percentage of basophilic granules are hardly shrunk allowing differentiation in sizes of leucocytes (see column 7, lines 36-47).

Sakata et al. differ in failing to disclose a nitrogenous compound in the reagent system.

Hamaguchi et al. has been discussed supra.

One of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success in incorporating the solubilizing agent / nitrogenous compound as taught by Hamaguchi into the reagent system taught by Sakata because Hamaguchi specifically disclosed and suggested applicability of such agent with all other reagents used in leucocyte classification such as the reagent system taught by Sakata.

Sakata et al. and Hamaguchi et al. differ in failing to disclose the specific concentration parameters of elements recited in claim 10-11.

It is, however, maintained that the concentration parameters such as detergent [0.2-20 g/l] and nitrogenous compound [0.1-10 g/l] recited in claim 10 and potassium chloride [5-15 g/l], 1,3- dimethyl-2- thiourea [0.5-5 g/l], dodecyltrimethylammonium chloride [0.5-5 g/l], and potassium hydrogen phosphate / HCl [1.0-10 g/l] which are

recited in claim 11, are all result effective variables which the prior art references have shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 10 and 11 are for any particular purpose or solve any stated problem and the prior art teaches that the different reagent elements and parameters often vary according to the sample being analyzed and parameters appear to work equally as well; absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the Sakata and Hamaguchi by normal optimization procedures known in the leucocyte differentiation art.

6. No claims are allowed.

Remarks

7. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Ledis et al. (US 4,286,963) disclose a lytic reagent diluent for 1) lysing red blood cells, 2) identifying and classifying lymphoid and myeloid populations in leucocytes, and 3) measuring hemoglobin content by rapid conversion and formation into chromogen in a blood sample (see Abstract and claim 1). Specifically, the reagent comprises a cationic detergent such as quaternary ammonium salt in high concentrations having attached to the nitrogen a long chain alkyl group conferring surface active properties, a buffer such as citric acid that maintains the pH to a desired pH of 3.5 - 5.0, and an additive comprising 1) a short chain alkanol substituted by phenyl or phenoxy and 2) a polyhydric alcohol compound to improve separation of leucocytes (see column 2, lines 51-64). According to Ledis, the lytic reagent can further be treated with alkaline buffered cyanide containing reagent to obtain satisfactory hemoglobin results (and column 4, lines 9-24).

Riesgo et al. (US 5,935,857) disclose a multipurpose blood diluent which allows determination of leucocyte subpopulations and hemoglobin parameters.

Li et al. (US 5,786,224) disclose a reagent composition capable of differentiation between five leucocyte subpopulations and determination of hemoglobin (see Example III and IX).

Lefevre et al. (US 5,196,346) disclose a reagent for automatically counting basophilic leucocytes in blood.

Uchihashi et al. (US 5,968,832) disclose a reagent for measurement of leucocytes and hemoglobin concentration including a cationic detergent and a hemoglobin stabilizer including sulfosalicylic acid, a chelating agent having a nitrogen compound, and a salt (see Abstract).

Cremins et al. (EPP 0 177 137) disclose compositions for leucocyte differentiation.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
June 24, 2001

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641